3:15 p.m.

848-6 **Aortic Valve Calcification and C-Reactive Protein Contribute Independently to Coronary Heart Disease Incidence**

Bobak Salami, Dave Shavelle, Min Xiang, Laurie LaBree, Stanley Azen, Miwa Kawakubo, Agnes Papa, Kevin O'Brien, Robert Detrano, Harbor-UCLA Research & Education Institue, Torrance, CA, University of Southern California, Los Angeles, CA

Background:
Recent studies suggest that inflammation and aortic valve calcium (AVC) play a role in the pathogenesis of subsequent cardiovascular events. We sought to determine whether C-reactive protein (CRP) and AVC are associated with events.
Methods:
858 non-diabetic participants in the South Bay Heart Watch without underlying coronary heart disease underwent baseline risk factor screening (including CRP levels) and non contrast gated computed tomography for AVC. Abnormal AVC was defined as > 75th percentile of the non zero values (>140 score units) and was present in 41 participants (4.8%). Mean follow-up was 7.0 +/- 0.5 years. AVC was measured using the method of the MESA study. Abnormal CRP was defined as > 75th percentile (>3.97 mg/L). Outcomes of non-fatal myocardial infarction, coronary death, coronary revascularization, or stroke were considered. Cox regression analysis was performed to determine the effect of AVC and CRP on clinical outcomes.
Results:
Results are shown in the table. Participants with both elevated AVC and CRP were more likely to suffer subsequent events than participants with only one of these findings (P=0.0004).
Conclusion:
A high AVC score in combination with elevated CRP in an asymptomatic person portends a higher risk for future cardiovascular events than either high AVC or CRP alone.

	CRP-, AVC-	CRP-, AVC+	CRP+, AVC-	CRP+, AVC+
RR	1.0	1.63	1.32	4.28
95% CI	---	0.70-3.79	0.86-2.02	1.92-9.57
P	---	0.26	0.21	0.0004

POSTER SESSION

1159

Vascular Function and Structure: Translational Research

Tuesday, March 09, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1159-183 **Circulating T Cell Perturbation and Macrophage Activation in Stable Coronary Artery Disease Patients: Effect of Atorvastatin Therapy**

Hannes F. Alber, Jakob Dörler, Matthias Frick, Wolfgang Dichtl, Ralf-Harun Zwick, Otmar Pachinger, Franz Weidinger, University Clinic of Innsbruck, Innsbruck, Austria

Background:
Coronary artery disease (CAD) is characterized by both T lymphocyte and macrophage activation. Statins have anti-inflammatory effects beyond lipid lowering. Whether these also affect the global immune system is unclear. The aim of this study was to investigate the influence of atorvastatin (atv) on circulating inflammatory T helper lymphocytes (TH_1), on their circulating activation marker soluble CD40 ligand (sCD40L), on the soluble intercellular adhesion molecule-1 (sICAM-1), involved in lymphocyte recruitment and on neopterin, a macrophage activation marker.
Methods:
30 hypercholesterolemic patients with angiographically documented stable CAD were randomized in a double-blind study to placebo or atv (20mg/d) for 3 months. Eight healthy volunteers served as controls. sCD40L, sICAM-1, neopterin and C-reactive protein (CRP) levels were measured with ELISA. TH_1 and anti-inflammatory T helper (TH_2) lymphocytes were characterized by intracellular staining of interleukin-2, specific for TH_1, and interleukin-4, specific for TH_2 cells, by FACS analysis.
Results:
TH_1 cells (47.9±10.8 vs 31.5±10.5%, p<0.002), neopterin (7.0±2.5 vs 4.5±1.3nmol/L, p<0.002), sCD40L (10.4± 4.5 vs 6.6±1.6ng/mL, p<0.01), sICAM-1 (251.8±83.6 vs 127.9± 58.7mg/dL, p<0.001) and CRP levels (0.47±0.40 vs 0.07±0.05mg/dL, p<0.001) were increased in CAD patients compared to controls. TH_2 cells were not different. LDL cholesterol was reduced by 37.3±16.5% in atv-treated patients (p<0.001) and by 8.2±15.7% (p=0.041) in the placebo group. TH_1 and TH_2 lymphocytes did not change in both groups. By contrast, neopterin (p<0.02), sCD40L (p<0.02), sICAM-1 (p<0.01) and CRP (p<0.01) were decreased in the atv group, but remained similar in the placebo group.
Conclusion:
Our data suggest that a *systemic* immune activation is present also in *stable* CAD patients. This activation is partially abolished by atorvastatin, supporting anti-inflammatory properties of this agent.

1159-184 **Maternal Undernutrition and Early Postnatal Diet Affect Aortic Structure and Composition in Rats**

Michael R. Skilton, Lisa M. Ho, Alison K. Gosby, Ian D. Caterson, David S. Celermajer, University of Sydney, Sydney, Australia

Many epidemiologic studies suggest a link between fetal and early infant nutrition, and predisposition to adult hypertension and coronary artery disease. We therefore examined the effects of altering nutrition during gestation, lactation, and then throughout juvenile life, on aortic structure and composition in rats.
Wistar rat dams were fed either a control (20% protein, 4% fat) or low protein (8% protein, 4% fat; LP) diet throughout pregnancy, or a low protein diet for the final 7 days of gestation only (LLP – last trimester low protein diet). At 21 days post-partum, 56 male pups were weaned onto a control, LP or high fat diet (20% protein, 25% fat). All diets were isocaloric. At 12 weeks, rats were euthanased, the thoracic aorta perfusion fixed in situ and then harvested. Aortic sections (6um thick) were stained with resorcin-fuchsin, to assess elastin content. Media thickness, lumen diameter and elastin content were measured using NIH Image software (blinded analysis).
Rats belonging to the maternal LP group had significantly reduced aortic lumen size (1.80 ± 0.03 vs 2.03 ± 0.05mm) and media thickness (128 ± 4 vs 143 ± 4um), when compared with controls (p<0.01). The maternal LLP group exhibited an increased percentage of elastin in the aortic wall (66 ± 1 vs 62 ± 1%, p<0.05) when compared with controls, while media thickness (137 ± 6um) and lumen diameter (2.10 ± 0.19mm) were unaffected. Regarding the effect of post-natal diet, low protein was associated with a further significant reduction in media thickness (p<0.05), but no change in lumen size or wall composition. A high fat diet after birth did not affect aortic parameters.
In conclusion, protein restriction throughout gestation results in significant reductions in aortic wall thickness and lumen size, exacerbated further by protein restriction after birth. These changes may contribute to the observed association between undernutrition in fetal/early life and vascular disease in adults.

1159-185 **Smoking-Related Endothelial Dysfunction and Increased Serum Levels of Proinflammatory Cytokines and Adhesion Molecules Are Reversible by Antioxidant Treatment**

Charalambos Antoniadis, Dimitrios Tousoulis, Marina Toutouza, Costas Tentolouris, Carmen Vasiliadou, Kyriakoula Marinou, Costas Tsioufis, Emmanuel Vavuranakis, Christos Pitsavos, Christodoulos Stefanadis, Athens Univeristy Medical School, Athens, Greece

Introduction: Smoking-related endothelial dysfunction and increased levels of interleukines 1b (IL-1b) and 6 (IL-6), tumor necrosis factor alpha (TNF-a), vascular cell adhesion molecule (sVCAM-1), intercellular adhesion molecule (sICAM-1) and lipid hydroperoxides (LPO), are implicated in atherogenesis. The effect of combined administration of vitamins C and E on endothelial function, lipid peroxidation and inflammatory process in smokers is unknown.
Methods: Forty-two healthy smokers (aged 36±2 yrs old) received vitamin C 2g/d (n=10, VITC), vitamin C 2g/d plus vitamin E 400IU/d (n=11, VITCE400), vitamin C 2g/d plus vitamin E 800IU/day (n=10, VITCE800) or no treatment (n=11, Controls), for 4 weeks. Forearm blood flow was measured using venous occlusion strain gauge plethysmography. Endothelium dependent dilation (EDD) and endothelium independent dilation were expressed as the %change of flow from rest to the maximum flow during reactive hyperemia or after sublingual nitroglycerine administration respectively. Inflammatory markers were determined with ELISA and LPO spectrocolorimetrically.
Results: EDD was increased in VITCE400 (46.5±5.4 to 74.3±9.2%, p<0.01) and VITCE800 (43.6±3.9 to 74.9±4.2%, p<0.001), but not in VITC and control groups. Similarly, LPO was reduced in VITCE400 and VITCE800 groups (14.5±1.2 and 15.4±2.9 to 8.8±1.6 and 8.3±1.7 μM respectively, p<0.05 for both) only. However, in VITCE800, a significant decrease was observed in levels of IL-1b (0.31±0.07 to 0.10±0.02 pg/ml, p<0.05), IL-6 (4.69±0.90 to 2.02±0.71 pg/ml,p<0.05), sVCAM-1 (339±14 to 298±11 ng/ml, p<0.05) and sICAM-1 (318±21 to 250±19 ng/ml, p<0.05), while TNF-a levels were slightly but not significantly decreased (1.76±0.343 to 1.27±0.074 pg/ml, p=NS). All the above parameters remained unchanged in VITC, VITCE400 and control groups.
Conclusions: Combined treatment with vitamins C (2g/day) and E (400 or 800IU/day), decreased lipid peroxidation and improved endothelial function in smokers. Combined administration of vitamins C (2g/d) and E (800IU/d) also decreased levels of IL-1b, IL-6, sVCAM-1 and sICAM-1 in these subjects.

1159-186 **High- but Not Low-Dose Folic Acid Improves Endothelial Function in Coronary Artery Disease**

Anil K. Madhavan, Stuart J. Moat, Ian F. McDowell, Malcolm J. Lewis, Jonathan Goodfellow, Derek Lang, Wales Heart Research Institute, Cardiff, United Kingdom

Background: Previous studies have demonstrated that high dose folic acid can improve endothelial function in coronary artery disease (CAD). However, the most efficacious dose of folic acid and the significance of homocysteine-lowering remain unclear. Therefore we sought to investigate the effects of both high dose (5mg/day) and low dose (400μg/day) folic acid supplementation on homocysteine-lowering and endothelial function in CAD.
Methods: 75 CAD patients entered a randomised, double blind, placebo controlled study comprising 3 parallel treatment groups (placebo, high and low dose folic acid). Endothelial function, assessed by flow-mediated dilatation (FMD) of the brachial artery, was measured before and after 6 weeks treatment. Plasma folate, B_{12}, total homocysteine, lipid profile, glucose and creatinine were also measured before and after treatment. All data are expressed as mean ± standard deviation.
Results: No significant changes in any parameters were observed in the placebo treated group. Treatment with high dose and low dose folic acid significantly (p<0.001) increased